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REQUEST FOR FILING A PATENT APPLICATION UNDER 37 CFR 1.60 (Small Entity)

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DOCKET NUMBER	ANTICIPATED CLASSIFICATION		PRIOR APPLICATION	
	CLASS	SUBCLASS		
M203C-D 36316.20332	606		08/485,821	3306

Address to:
Assistant Commissioner for Patents
Washington, D.C. 20231

This is a request for filing a ☒ continuation ☐ divisional application under 37 CFR 1.60 of pending prior application, Serial Number **08/485,821** filed on **June 6, 1995** and entitled:

Endovascular Electrolytically Detachable Wire and Tip for the Formation of Thrombus in Arteries, Veins, Aneurysms, Vascular Malformations and Arteriovenous Fistulas

1. Enclosed is a copy of the latest inventor-signed prior application, including a copy of the oath or declaration showing the original signature or an indication it was signed. I hereby verify that the attached papers are a true copy of the latest signed prior application, Serial Number **08/485,821**, and further that all statements made herein of my own knowledge are true; and further that these statements were made with the knowledge that willful false statements and the like are made punishable by fine or imprisonment or both, under section 1001 of Title 18 of the United States Code and that such willful statements may jeopardize the validity of the application or any patent issuing thereon.

CLAIMS AS FILED

For	#Filed	#Allowed	#Extra	Rate	Fee
Total Claims	2	- 20 =	0	x $11.00	$0.00
Indep. Claims	2	- 3 =	0	x $40.00	$0.00
Multiple Dependent Claims (check if applicable)			☐		$0.00
				BASIC FEE	$385.00
				TOTAL FILING FEE	$385.00

2. ☒ A verified statement to establish small entity status under 37 CFR 1.9 and 1.27
   - ☐ is enclosed.
   - ☒ was filed in prior application Serial Number **08/485,821** and such status is still proper and desired (37 CFR 1.28(a)).

3. ☒ The Commissioner is hereby authorized to charge any fees which may be required under 37 CFR 1.16 and 1.17, or credit any overpayment to Deposit Account No. **04-0259** A duplicate copy of this sheet is enclosed.

4. ☒ A check in the amount of **$385.00** is enclosed.

5. ☒ Cancel in this application original claims **2-6 and 8-24** of the prior application before calculating the filing fee. (At least one original independent claim must be retained for filing purposes.)

6. ☒ Amend the specification by inserting before the first line the sentence: "This application is a ☒ continuation ☐ division of application Serial Number **08/485,821** filed **June 6, 1995** which application is now:
   - ☐ abandoned.
   - ☒ pending.
   - ☐ other (explain):

7. ☒ Transfer the drawings from the pending prior application to this application and abandon said prior application as of the filing date accorded this application. A duplicate copy of this sheet is enclosed for filing in the prior application. (May only be used if signed by person authorized by 37 CFR 1.138 and before payment of issue fee.)

REQUEST FOR FILING A PATENT APPLICATION UNDER 37 CFR 1.60
(Small Entity)

8. ☐ New formal drawings are enclosed.

9. ☐ Priority of foreign application number _____ filed on _____ in _____ (*Country*) is claimed under 35 U.S.C. 119.
   ☐ The certified copy has been filed in prior application Serial Number _____ filed on _____

10. ☐ A preliminary amendment is enclosed.

11. ☒ The prior application is assigned of record to:
Target Therapeutics and the Regents of the University of California

12. ☐ Also enclosed:

13. ☒ The power of attorney in the prior application is to:
Daniel L. Dawes

a. ☒ The power of attorney appears in the original papers in the prior application.

b. ☐ Since the power of attorney does not appear in the original papers, a copy of the power of attorney in the prior application is enclosed.

c. ☒ Address all future correspondence to: (May only be completed by applicant, or attorney or agent of record.)
Daniel L. Dawes
5252 Kenilworth Drive
Huntington Beach, CA 92649

Dated: **February 14 1997**

_____
Signature

Daniel L. Dawes
Typed or printed name

27,123
Registration Number (if applicable)

☐ Inventor(s)
☐ Assignee of complete interest
☒ Attorney or agent of record
☐ Filed under 37 C.F.R. 1.34(a)

cc: **University of California, Office of Technology Transfer**

CERTIFICATE OF MAILING BY "EXPRESS MAIL" (37 CFR 1.10) Applicant(s): **Guido Guglielmi and Ivan Sepetka**			Docket No. **M203e-D 36316.20332**
Serial No. **Unknown**	Filing Date **Herewith**	Examiner **L. Cohen**	Group Art Unit **3305**

Invention: **Endovascular Electrolytically Detachable Wire and Tip for the Formation of Thrombus in Arteries, Veins, Anuerysms. Vascular Malformations and Arteriovenous Fistulas**

I hereby certify that this **37 CFR 1.60 request and the documents referred to as attached therein**
(Identify type of correspondence)

is being deposited with the United States Postal Service "Express Mail Post Office to Addressee" service under 37 CFR 1.10 in an envelope addressed to: The Assistant Commissioner for Patents, Washington, D.C. 20231 on

February 14, 1997
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Lori M. Tillman
(Typed or Printed Name of Person Mailing Correspondence)

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IMPROVEMENTS IN AN ENDOVASCULAR ELECTROLYTICALLY DETACHABLE WIRE AND TIP FOR THE FORMATION OF THROMBUS IN ARTERIES, VEINS, ANEURYSMS, VASCULAR MALFORMATIONS AND ARTERIOVENOUS FISTULAS

This application is a continuation-in-part application of United States Patent Application Serial No. 07/492,717, filed March 13, 1990, and assigned to the same assignees as the present application, issued _____ as U.S. Patent _____.

Background of the Invention

1. Field of the Invention

The invention relates to a method and apparatus for endovascular electrothrombic formation of thrombi in arteries, veins, aneurysms, vascular malformations and arteriovenous fistulas.

2. Description of the Prior Art

Approximately 25,000 intracranial aneurysms rupture every year in North America. The primary purpose of treatment for ruptured intracranial aneurysm is to prevent rebleeding. At the present time, three general methods of treatment exist, namely an extravascular, endovascular and extra-endovascular approach.

The extravascular approach is comprised of surgery or microsurgery of the aneurysm or treatment site for the purpose of preserving the parent artery. This treatment is common with intracranial berry aneurysms. The methodology comprises the step of clipping the neck of the aneurysm, performing a suture-ligation of the neck, or wrapping the entire aneurysm. Each of these surgical procedures is performed by intrusive invasion into the body and performed from outside the aneurysm or target site. General anesthesia, craniotomy, brain retraction and arachnoid dissection around the neck of the aneurysm and placement of a clip are typically required in these surgical procedures. Surgical treatment of vascular intracranial aneurysm can expect a mortality rate of 4-8% with a morbidity rate of 18-20%. Because of the mortality and morbidity rate expected, the surgical procedure is often delayed while waiting for the best surgical time with the result that an additional percentage of patients will die from the underlying disease or defect prior to surgery. For this reason the prior art has sought alternative means of treatment.

In the endovascular approach, the interior of the aneurysm is entered through the use of a microcatheter. Recently developed microcatheters, such as those shown by **Engelson**, *"Catheter Guidewire"*, U.S. Patent 4,884,579 and as

described in **Engelson**, *"Catheter for Guidewire Tracking"*, U.S. Patent 4,739,768 (1988), allow navigation into the cerebral arteries and entry into a cranial aneurysm.

In such procedures a balloon is typically attached to the end of the microcatheter and it is possible to introduce the balloon into the aneurysm, inflate it, and detach it, leaving it to occlude the sac and neck with preservation of the parent artery. While endovascular balloon embolization of berry aneurysms is an attractive method in situations where an extravascular surgical approach is difficult, inflation of a balloon into the aneurysm carries some risk of aneurysm rupture due to possible over-distention of portions of the sac and due to the traction produced while detaching the balloon.

While remedial procedures exist for treating a ruptured aneurysm during classical extravascular surgery, no satisfactory methodology exists if the aneurysm breaks during an endovascular balloon embolization.

Furthermore, an ideal embolizing agent should adapt itself to the irregular shape of the internal walls of the aneurysm. On the contrary, in a balloon embolization the aneurysmal wall must conform to the shape of the balloon. This may not lead to a satisfactory result and further increases the risk of rupture.

Still further, balloon embolization is not always possible. If the diameter of the deflated balloon is too great to enter the intracerebral arteries, especially in the cases where there is a vasospasm, complications with ruptured intracranial aneurysms may occur. The procedure then must be deferred until the spasm is resolved and this then incurs a risk of rebleeding.

In the extra-intravascular approach, an aneurysm is surgically exposed or stereotaxically reached with a probe. The wall of the aneurysm is then perforated

from the outside and various techniques are used to occlude the interior in order to prevent it from rebleeding. These prior art techniques include electrothrombosis, isobutyl-cyanoacrylate embolization, hog-hair embolization and ferromagnetic thrombosis.

In the use of electrothrombosis for extra-intravascular treatment the tip of a positively charged electrode is inserted surgically into the interior of the aneurysm. An application of the positive charge attracts white blood cells, red blood cells, platelets and fibrinogen which are typically negatively charged at the normal pH of the blood. The thrombic mass is then formed in the aneurysm about the tip. Thereafter, the tip is removed. See **Mullan**, *"Experiences with Surgical Thrombosis of Intracranial Berry Aneurysms and Carotid Cavernous Fistulas"*, J. Neurosurg., Vol. 41, December 1974; **Hosobuchi**, *"Electrothrombosis Carotid-Cavernous Fistula"*, J. Neurosurg., Vol. 42, January 1975; **Araki et al.**, *"Electrically Induced Thrombosis for the Treatment of Intracranial Aneurysms and Angiomas"*, Excerpta Medica International Congress Series, Amsterdam 1965, Vol. 110, 651-654; **Sawyer et al.**, *"Bio-Electric Phenomena as an Etiological Factor in Intravascular Thrombosis"*, Am. J. Physiol., Vol. 175, 103-107 (1953); **J. Piton et al.**, *"Selective Vascular Thrombosis Induced by a Direct Electrical Current; Animal Experiments"*, J. Neuroradiology, Vol. 5, pages 139-152 (1978). However, each of these techniques involves some type of intrusive procedure to approach the aneurysm from the exterior of the body.

The prior art has also devised the use of a liquid adhesive, isobutyl-cyanoacrylate (IBCA) which polymerizes rapidly on contact with blood to form a firm mass. The liquid adhesive is injected into the aneurysm by puncturing the sac with a small needle. In order to avoid spillage into the parent artery during IBCA

injection, blood flow through the parent artery must be momentarily reduced or interrupted. Alternatively, an inflated balloon may be placed in the artery at the level of the neck of the aneurysm for injection. In addition to the risks caused by temporary blockage of the parent artery, the risks of seepage of such a polymerizing adhesive into the parent artery exists, if it is not completely blocked with consequent occlusion of the artery.

Still further, the prior art has utilized an air gun to inject hog hair through the aneurysm wall to induce internal thrombosis. The success of this procedure involves exposing the aneurysm sufficiently to allow air gun injection and has not been convincingly shown as successful for thrombic formations.

Ferromagnetic thrombosis in the prior art in extra-intravascular treatments comprises the stereotactic placement of a magnetic probe against the sac of the aneurysm followed by injection into the aneurysm by an injecting needle of iron microspheres. Aggregation of the microspheres through the extravascular magnet is followed by interneuysmatic thrombus. This treatment has not been entirely successful because of the risk of fragmentation of the metallic thrombus when the extravascular magnet is removed. Suspension of the iron powder in methyl methymethacrylate has been used to prevent fragmentation. The treatment has not been favored, because of the need to puncture the aneurysm, the risk of occlusion of the parent artery, the use of unusual and expensive equipment, the need for a craniectomy and general anesthesia, and the necessity to penetrate cerebral tissue to reach the aneurysm.

Endovascular coagulation of blood is also well known in the art and a device using laser optically generated heat is shown by O'Reilly, *"Optical Fiber with*

Attachable Metallic Tip for Intravascular Laser Coagulation of Arteries, Veins, Aneurysms, Vascular Malformation and Arteriovenous Fistulas", U.S. Patent 4,735,201 (1988). See also, **O'Reilly et al.,** *"Laser Induced Thermal Occlusion of Berry Aneurysms: Initial Experimental Results"*, Radiology, Vol. 171, No. 2, pages 471-74 (1989). **O'Reilly** places a tip into an aneurysm by means of an endovascular microcatheter. The tip is adhesively bonded to a optic fiber disposed through the microcatheter. Optical energy is transmitted along the optic fiber from a remote laser at the proximal end of the microcatheter. The optical energy heats the tip to cauterize the tissue surrounding the neck of the aneurysm or other vascular opening to be occluded. The catheter is provided with a balloon located on or adjacent to its distal end to cut off blood flow to the site to be cauterized and occluded. Normally, the blood flow would carry away the heat at the catheter tip, thereby preventing cauterization. The heat in the tip also serves to melt the adhesive used to secure the tip to the distal end of the optical fiber. If all goes well, the tip can be separated from the optical fiber and left in place in the neck of the aneurysm, provided that the cauterization is complete at the same time as the hot melt adhesive melts.

A thrombus is not formed from the heated tip. Instead, blood tissue surrounding the tip is coagulated. Coagulation is a denaturation of protein to form a connective-like tissue similar to that which occurs when the albumen of an egg is heated and coagulates from a clear running liquid to an opaque white solid. The tissue characteristics and composition of the coagulated tissue is therefore substantially distinct from the thrombosis which is formed by the thrombotic aggregation of white and red blood cells, platelets and fibrinogen. The coagulative

tissue is substantially softer than a thrombic mass and can therefore more easily be dislodged.

O'Reilly's device depends at least in part upon the successful cauterization timed to occur no later than the detachment of the heat tip from the optic fiber. The heated tip must also be proportionally sized to the neck of the aneurysm in order to effectively coagulate the tissue surrounding it to form a blockage at the neck. It is believed that the tissue in the interior of the aneurysm remains substantially uncoagulated. In addition, the hot melt adhesive attaching the tip to the optic fiber melts and is dispersed into the adjacent blood tissue where it resolidifies to form free particles within the intracranial blood stream with much the same disadvantages which result from fragmentation of a ferromagnetic electrothrombosis.

Therefore, what is needed is an apparatus and methodology which avoids each of the shortcomings and limitations of the prior art discussed above.

Brief Summary of the Invention

The invention is a method for forming an occlusion within a vascular cavity having blood disposed therein comprising the steps of endovascularly disposing a wire and/or tip near an endovascular opening into the vascular cavity. The wire may include a distinguishable structure at its distal end, which is termed a tip, in which case the remaining portion of the wire may be termed a guidewire. The term "wire" should be understood to collectively include both guidewires and tips and simply wires without distinct tip structures. However, the tip may also simply be the extension of the wire itself without substantial distinction in its nature. A distal tip

of the wire is disposed into the vascular cavity to pack the cavity to mechanically form the occlusion within the vascular cavity about the distal tip. The distal tip is detached from the guidewire (or wire) to leave the distal tip within the vascular cavity. As a result, the vascular cavity is occluded by the distal tip, and by any thrombus formed by use of the tip.

In one embodiment, the step of detaching the distal tip from the guidewire (or wire) comprises the step of mechanically detaching the distal tip from the guidewire (or wire).

In another embodiment, the guidewire and tip (or wire) are used within a microcatheter and in the step of detaching the distal tip from the guidewire (or wire), the guidewire and tip (or wire) are longitudinally displaced within the microcatheter. The microcatheter has radio-opaque proximal and tip markers. The guidewire and tip (or wire) have collectively a single radio-opaque marker. The displacement of the guidewire and tip (or wire) moves the single radio-opaque marker to the proximity of the proximal marker on the microcatheter. At this point the tip will be fully deployed in the vascular cavity and tip separation may proceed. It is not necessary then in this embodiment to be able to see actual deployment of the tip before separation. The tip marker allows and enhances direct observation of the correct placement of the catheter tip into the opening of the vascular cavity.

In one embodiment the step of disposing the tip (or wire) into the vascular cavity to pack the cavity comprises the step of disposing a tip (or wire) having a plurality of filaments extending therefrom to pack the cavity.

In another embodiment the step of disposing the tip (or wire) into the vascular cavity to pack the cavity comprises the step of disposing a long flexible tip (or wire) folded upon itself a multiple number of times to pack the cavity.

The invention can also be characterized as a method for forming an occlusion within a vascular cavity having blood disposed therein comprising the steps of endovascularly disposing a wire within a microcatheter near an endovascular opening into the vascular cavity. The microcatheter has a distal tip electrode. The distal tip of the wire is disposed into the vascular cavity to pack the cavity to form the occlusion within the vascular cavity about the distal tip of the wire by applying a current between the distal tip electrode and the distal end of the wire packed into the cavity. The distal tip of the wire is detached from the wire to leave the distal tip of the wire within the vascular cavity. As a result, the vascular cavity is occluded by the distal tip, and by any thrombus formed by use of the tip.

The invention is also a wire for use in formation of an occlusion within a vascular cavity used in combination with a microcatheter comprising a core wire, and a detachable elongate tip portion extending the core wire for a predetermined lineal extent. The tip portion is adapted to be packed into the vascular cavity to form the occlusion in the vascular cavity and coupled to the distal portion of the core wire. As a result, endovascular occlusion of the vascular cavity can be performed.

In one embodiment, the elongate tip portion is a long and substantially pliable segment adapted to be multiply folded upon itself to substantially pack said vascular cavity.

In another embodiment, the elongate tip portion is a segment adapted to be disposed in said vascular cavity and having a plurality of filaments extending therefrom to substantially pack said vascular cavity when disposed therein.

In still another embodiment, the microcatheter has a pair of radioopaque markers disposed thereon and the core wire has a radioopaque marker disposed thereon. The marker on the core wire is positioned in the proximity of one of the pair of markers on the microcatheter when the core wire is fully deployed. The other marker on the core wire marks the position of the catheter tip.

The invention is still further characterized as a microcatheter system for use in formation of an occlusion within a vascular cavity comprising a microcatheter having a distal end adapted for disposition in the proximity of the vascular cavity. The distal end has an electrode disposed thereon. A conductive guidewire is disposed in the microcatheter and longitudinally displaceable therein. The guidewire comprises a core wire, and an elongate tip portion extending the core wire for a predetermined lineal extent. The tip portion is adapted to be packed into the vascular cavity to form the occlusion in the vascular cavity. The tip portion is coupled to the distal portion of the core wire. The occlusion is formed by means of applying a current between the tip portion and the electrode on the microcatheter when the tip portion is disposed into the vascular cavity. As a result, endovascular occlusion of the vascular cavity can be performed.

More generally speaking, the invention is a method for forming an occlusion within a vascular cavity having blood disposed therein comprising the steps of disposing a body into the cavity to substantially impede movement of blood in the

cavity. The body is employed in the cavity to form the occlusion within the vascular cavity. As a result, the vascular cavity is occluded by the body.

The step of disposing the body in the vascular cavity comprises the step of packing the body to substantially obstruct the cavity.

In one embodiment the step of packing the cavity with the body comprises the step of obstructing the cavity with a detachable elongate wire tip multiply folded upon itself in the cavity.

The step of disposing the body into the vascular cavity comprises disposing in the vascular cavity means for slowing blood movement in the cavity to initiate formation of the occlusion in the cavity.

In another embodiment the step of packing the cavity with the body comprises the step of obstructing the cavity with a body having a compound filamentary shape.

The step of employing the body in the vascular cavity to form the occlusion comprises the step of applying an electrical current to the body or mechanically forming the occlusion in the body or both simultaneously.

The invention is also wire for use in formation of an occlusion within a vascular cavity used in combination with a microcatheter. The invention comprises a core wire and a detachable elongate tip portion extending the core wire for a predetermined lineal extent. The core wire is adapted to being packed into the vascular cavity to form the occlusion in the vascular cavity and is coupled to the distal portion of the core wire. The tip portion includes a first segment for disposition into the cavity and a second segment for coupling the first portion to the core wire. The second segment is adapted to be electrolysized upon application of

current. An insulating coating is disposed on the first segment. The second segment is left exposed to permit selective electrolysis thereof. As a result, endovascular occlusion of the vascular cavity can be performed.

The invention can better be visualized by now turning to the following drawings wherein like elements are referenced by like numerals.

Brief Description of the Drawings

Figure 1 is an enlarged partially cross-sectioned side view of a first embodiment of the distal end of the guidewire and tip of the invention.

Figure 2 is an enlarged longitudinal cross section of a second embodiment of the guidewire and tip of the invention.

Figure 3 is an enlarged side view of a third embodiment of the invention with a microcatheter portion cut away in a longitudinal cross-sectional view.

Figure 4 is a simplified depiction of the wire of Figure 3 shown disposed within a simple cranial aneurysm.

Figure 5 is a depiction of the wire of Figure 4 shown after electrolytic detachment of the tip.

Figure 6 is a plan view of another embodiment of the guidewire and tip portion wherein the type is provided with a plurality of polyester filamentary hairs.

Figures 7 and 8 are a diagrammatic depictions of the use of the invention wherein position markers have been provided on the catheter and wire to assist in proper fluoroscopic manipulation.

Figure 9 is a simplified cross-sectional view of the catheter and wire showing a ground electrode disposed on the distal tip of the catheter.

The invention and its various embodiments are best understood by now turning to the following detailed description.

Detailed Description of the Preferred Embodiments

An artery, vein, aneurysm, vascular malformation or arterial fistula is occluded through endovascular occlusion by the endovascular insertion of a platinum tip into the vascular cavity. The vascular cavity is packed with the tip to obstruct blood flow or access of blood in the cavity such that the blood clots in the cavity and an occlusion if formed. The tip may be elongate and flexible so that it packs the cavity by being folded upon itself a multiple number of times, or may pack the cavity by virtue of a filamentary or fuzzy structure of the tip. The tip is then separated from the wire mechanically or by electrolytic separation of the tip from the wire. The wire and the microcatheter are thereafter removed leaving the tip embedded in the thrombus formed within the vascular cavity. Movement of wire in the microcatheter is more easily tracked by providing a radioopaque proximal marker on the microcatheter and a corresponding indicator marker on the wire. Electrothrombosis is facilitate by placing the ground electrode on the distal end of the microcatheter and flowing current between the microcatheter electrode and the tip.

When the tip is separated from the wire by electrolytic separation of the tip from the wire, a portion of the wire connected between the tip and the body of the wire is comprised of stainless steel and exposed to the bloodstream so that upon continued application of a positive current to the exposed portion, the exposed portion is corroded away at least at one location and the tip is separated from the body of the wire.

Figure 1 is an enlarged side view of a first embodiment of the distal end of the wire and tip shown in partial cross-sectional view. A conventional Teflon

laminated or similarly insulated stainless steel wire 10 is disposed within a protective microcatheter (not shown). Stainless steel wire 10 is approximately 0.010 - 0.020 inch (0.254-0.508 mm) in diameter. In the illustrated embodiment, wire 10 is tapered at its distal end to form a conical section 12 which joins a section 14 of reduced diameter which extends longitudinally along a length 16 of wire 10. Section 16 then narrows gradually down to a thin threadlike portion 18 beginning at a first bonding location 20 and ending at a second bonding location 22.

The stainless steel wire 10, comprised of that portion disposed within the microcatheter body, tapered section 12, reduced diameter section 16 and threadlike section 18, is collectively referred to as a core wire which typically is 50 - 300 cm. in length.

In the illustrated embodiment the portion of the core wire extending from tapered section 12 to second bonding location 22 is collectively referred to as the grinding length and may typically be between 20 and 50 cm. in length.

Reduced diameter portion 14 and at least part of sections 12 and first bonding location 20 may be covered with an insulating Teflon laminate 24 which encapsulates the underlying portion of wire 10 to prevent contact with the blood.

A stainless steel coil 26 is soldered to the proximate end of threadlike portion 18 of wire 10 at first bonding location 20. Stainless steel coil 26 is typically 3 to 10 cm. in length and like wire 10 has a diameter typically between 0.010 to 0.020 inch (0.254-0.508 mm).

The distal end of stainless steel coil 26 is soldered to the distal end of threadlike portion 18 of wire 10 and to the proximal end of a platinum secondary coil 28 at second bonding location 22. Secondary coil 28 itself forms a spiral or helix

typically between 2 to 10 mm. in diameter. The helical envelope formed by secondary coil 28 may be cylindrical or conical. Like wire 10 and stainless steel coil 26, secondary coil 28 is between approximately 0.010 and 0.020 inch (0.254-0.508 mm) in diameter. The diameter of the wire itself forming stainless steel coil 26 and coil 28 is approximately between 0.001 - 0.005 inch.

The distal end of secondary coil 28 is provided with a platinum soldered tip 30 to form a rounded and smooth termination to avoid puncturing the aneurysm or tearing tissue.

Although prebiased to form a cylindrical or conical envelope, secondary coil 28 is extremely soft and its overall shape is easily deformed. When inserted within the microcatheter (not shown), secondary coil 28 is easily straightened to lie axially within the microcatheter. Once disposed out of the tip of the microcatheter, secondary coil 28 forms the shape shown in Figure 1 and may similarly be loosely deformed to the interior shape of the aneurysm.

As will be described below in greater detail in connection with the third embodiment of Figure 3, after placement of secondary coil 28 within the interior of the aneurysm, a direct current is applied to wire 10 from a voltage source exterior to the body. The positive charge on secondary coil 28 within the cavity of the aneurysm causes a thrombus to form within the aneurysm by electrothrombosis. Detachment of the tip occurs either: (1) by continued application of current for a predetermined time when the portion 18 is exposed to blood; or (2) by movement of the wire to expose portion 18 to blood followed by continued current application for a predetermined time. Ultimately, both threadlike portion and stainless steel coil 26 will be completely disintegrated at least at one point, thereby allowing wire 10 to

be withdrawn from the vascular space while leaving secondary coil 28 embedded within the thrombus formed within the aneurysm.

Figure 2 illustrates in enlarged partially cross-sectional view a second embodiment of the invention. Stainless steel core 32 terminates in a conical distal portion 34. Stainless steel coil 36, shown in cross-sectional view, is soldered to distal portion 34 of wire 32 at bonding location 38. The opposing end of the stainless steel coil 36 is provided with a soldered, rounded platinum tip 40. In the illustrated embodiment, stainless steel core wire 32 is approximately 0.010 inch in diameter with the length of stainless steel coil 36 being approximately 8 cm. with the longitudinal length of platinum tip 40 being between 3 and 10 mm. The total length of wire 32 from tip 40 to the proximate end is approximately 150 cm.

The embodiment of Figure 2 is utilized in exactly the same manner as described above in connection with Figure 1 to form a thrombic mass within an aneurysm or other vascular cavity. The embodiment of Figure 2 is distinguished from that shown in Figure 1 by the absence of the extension of stainless core 32 through coil 36 to tip 40. In the case of the embodiment of Figure 2 no inner core or reinforcement is provided within stainless steel coil 36. Threadlike portion 18 is provided in the embodiment of Figure 1 to allow increased tensile strength of the wire. However, a degree of flexibility of the wire is sacrificed by the inclusion even of threadlike tip 18, so that the embodiment of Figure 2 provides a more flexible tip, at least for that portion of the micro-guidewire constituting the stainless steel coil 36.

It is expressly understood that the helical secondary coil tip of the embodiment of Figure 1 could similarly be attached to stainless steel coil 36 of the

embodiment of Figure 2 without departing from the spirit and scope of the invention.

Thinned and threadlike portion guidewires disposed concentrically within coiled portions are well known and are shown in **Antoshkiw**, *"Disposable Guidewire"*, U.S. Patent 3,789,841 (1974); **Sepetka et al.**, *"Guidewire Device"*, U.S. Patent 4,832,047 (1989); **Engelson**, *"Catheter Guidewire"*, U.S. Patent 4,884,579 (1989); **Samson et al.**, *"Guidewire for Catheters"*, U.S. Patent 4,538,622 (1985); and **Samson et al.**, *"Catheter Guidewire with Short Spring Tip and Method of Using the Same"*, U.S. Patent 4,554,929 (1985).

Turn now to the third embodiment of the invention as shown in Figure 3. Figure 3 shows an enlarged side view of a wire, generally denoted by reference numeral 42, disposed within a microcatheter 44 shown in cross-sectional view. Like the embodiment of Figure 1, a stainless steel coil 46 is soldered to a conical portion 48 of wire 22 at a first bonding location 50. A thin threadlike extension 52 is then longitudinally disposed within stainless steel coil 46 to a second bonding location 54 where stainless steel wire 46 and threadlike portion 52 are soldered to a soft platinum coil 56. Platinum coil 56 is not prebiased, nor does it contain any internal reinforcement, but is a free and open coil similar in that respect to stainless steel coil 36 of the embodiment of Figure 2.

However, platinum coil 56 is particularly distinguished by its length of approximately 1 to 50 cm. and by its flexibility. The platinum or platinum alloy used is particularly pliable and the diameter of the wire used to form platinum coil 56 is approximately 0.001 - 0.005 inch in diameter. The distal end of platinum coil 56 is

provided with a smooth and rounded platinum tip 58 similar in that respect to tips 30 and 40 of Figures 1 and 2, respectively.

When coil 56 is disposed within microcatheter 44, it lies along the longitudinal lumen 60 defined by microcatheter 44. The distal end 62 of microcatheter 60 is then placed into the neck of the aneurysm and the wire 42 is advanced, thereby feeding tip 58 in platinum coil 56 into aneurysm 64 until bonding location 50 resides in the neck of the aneurysm as best depicted in the diagrammatic cross-sectional view of Figure 4.

Figure 4 illustrates the insertion of the embodiment of Figure 3 within a vessel 66 with distal tip of microcatheter 44 positioned near neck 68 of aneurysm 64. Coil 56 is fed into aneurysm 64 until at least a portion of stainless steel coil 46 is exposed beyond the distal tip 62 of microcatheter 44. A positive electric current of approximately 0.01 to 2 milliamps at 0.1 - 6 volts is applied to wire 42 to form the thrombus. Typically a thrombus will form within three to five minutes. The negative pole 72 of voltage source 70 is typically placed over and in contact with the skin.

After the thrombus has been formed and the aneurysm completely occluded, tip 58 and coil 56 are detached from wire 42 by electrolytic disintegration of at least one portion of stainless steel coil 46. In the illustrated embodiment this is accomplished by continued application of current until the total time of current application is almost approximately four minutes.

At least one portion of stainless steel coil 46 will be completely dissolved through by electrolytic action within 3 to 10 minutes, usually about 4 minutes. After separation by electrolytic disintegration, wire 42, microcatheter 44 and the

remaining portion of coil 46 still attached to wire 42 are removed from vessel 66, leaving aneurysm 64 completely occluded as diagrammatically depicted in Figure 5 by thrombus 74. It will be appreciated that the time of disintegration may be varied by altering the dimensions of the portions of the wire and/or the current.

The process is practiced under fluoroscopic control with local anesthesia at the groin. A transfemoral microcatheter is utilized to treat the cerebral aneurysm. The platinum is not affected by electrolysis and the remaining portions of the microcatheter are insulated either by a Teflon lamination directly on wire 42 and/or by microcatheter 44. Only the exposed portion of the wire 46 is affected by the electrolysis.

It has further been discovered that thrombus 74 continues to form even after detachment from wire 42. It is believed that a positive charge is retained on or near coil 56 which therefore continues to attract platelets, white blood cells, red blood cells and fibrinogen within aneurysm 64.

Although the foregoing embodiment has been described as forming an occlusion within a blood-filled vascular cavity by means of electrothrombosis, the above disclosure must be read to expressly include formation of the occlusion by mechanical mechanisms without resort to the application of electrical current. A mechanical mechanism which can be safely disposed into the vascular cavity to impede, slow or otherwise initiate clotting of the blood or formation of the occlusion is within the scope of the invention. The insertion within the vascular cavity and maintenance therein of an object with an appropriate blood-clotting characteristics can and does in many cases cause the formation of an occlusion by itself. Depicted in Figure 6 is an embodiment of the invention wherein such mechanical thrombosis

can be achieved. Wire 10 has a tapering end portion 14 covered with a Teflon laminate 24 similar to that described in connection with the embodiment of Figure 1. Wire 10 is attached by means of a mechanical coupling 100 to a platinum coil 102 which has a plurality of filaments or fine hairs 104 extending therefrom. In the illustrated embodiment, hairs 104 have a length as may be determined from the size of the vascular cavity in which coil 102 is to be used. For example, in a small vessel hair lengths of up to 1 mm are contemplated. An example of polyester filaments or hairs attached to a coil which was not used in electrothrombosis may be seen in the copending application entitled Vasoocclusion Coil with Attached Fiberous Elements, filed Oct. 2, 1991, serial number 07/771,013.

Coil 102 has sufficient length and flexibility that it can be inserted or coiled loosely into the vascular cavity. The length of coil 102 need not be so long that the coil itself is capable of being multiply folded on itself and fill or substantially fill the vascular cavity. Hairs 104 extending from coil 102 serve to substantially pack, fill or at least impede blood flow or access in the vascular cavity. Hairs 104, which are generally inclined backwardly away from extreme tip 106 when delivered, are thus easily able to slide forward with little friction through restrictions in the vessels and aneurysm. Additionally, hairs 104 do not have sufficient length, strength or sharpness to provide any substantial risk or potential for a puncture of the thin vascular wall. The plurality of hairs 104, when coiled within the vascular cavity, provide an extremely large surface for attachment of blood constituents to encourage and enhance the formation of a mechanical occlusion within the vascular opening.

In the preferred embodiment, coil 102 is mechanically coupled to thin tapered portion 104 of wire 10 by means of a small drop of polyester 100. Polyester may be substituted for the gold solder of the previously described embodiments in order to reduce concern or risk of toxic reactions in the body.

Tip portion 104 may also be mechanically separated from wire 10 by means other than electrolysis. One method is make the connection between tip 104 and wire 10 by means of a spring loaded mechanical clasp (not shown). The clasps are retained on tip 104 as long as the clasps remain inside of the catheter, but spring open and release tip 104 when extended from the catheter. The catheter and clasps may then be removed from the insertion site. This type of mechanical connection is described in the copending application entitled, "Detachable Pusher-Vasoocclusive Coil Assembly with Interlocking Coupling", filed Dec. 12, 1991 with serial number 07/806,979 which is incorporated herein by reference and assigned to Target Therapeutics Inc. An alternative nonresilient mechanical ball and clasp capturing mechanism is described in the copending application entitled "Detachable Pusher-Vasoocclusive Coil Assembly with Interlocking Ball and Keyway Coupling", filed Dec. 12, 1991 with serial number 07/806,912 which is also incorporated herein by reference and assigned to Target Therapeutics Inc.

In another embodiment wire 10 and tip portion 104 screw into each other and can be unscrewed from each other by rotation of the catheter or wire with respect to tip 104. An extendable sheath (not shown) in the microcatheter is advanced to seize tip 104 to prevent its rotation with wire 10 during the unscrewing process. This type of mechanical connection is described in the copending application entitled "Detachable Pusher-Vasoocclusive Coil Assembly with

Threaded Coupling", filed Dec. 12, 1991 with serial number 07/806,878 which is incorporated herein by reference and assigned to Target Therapeutics Inc.

In any case the specific means disclosed here of mechanically detaching tip 104 from wire 10 forms no part of the present invention apart from its combination as a whole with other elements of the invention. Specific disclosure of the mechanical means of detachment have been set forth only for the purposes of providing an enabling disclosure of the best mode presently known for practicing the claimed invention.

Even where the occlusion is not formed by electrothrombosis, separation of tip 104 may be effected by electrolysis. In such situations, the electrolysing current may be concentrated on the sacrificial stainless steel portion of tip 104 by disposition of an insulative coating on the remaining platinum portion. For example, tip 104 may be provided with a polyethylene coating save at least a portion of the stainless steel length. This has the effect of decreasing the time required to electrolytically sufficiently disintegrate the steel portion to allow detachment of the platinum tip, which is an advantageous feature in those cases where a large aneurysm must be treated and a multiple number of coils must be deployed within the aneurysm.

Notwithstanding the fact that wire 10 and platinum coil 102 in the embodiment Figure 6 or wire 10 and platinum coil 28, 36 and 56 in the embodiments of Figures 1-5 are radiopaque, there is still some difficulty when manipulating the device under fluoroscopy to be able to determine the exact position or movement of the probe relative to the aneurysm. This is particularly true when a large number of coils are deployed and one coil then radiographically

hides another. Figure 7 illustrates an improvement of, for example, the embodiment of Figures 4 and 5. Microcatheter 144 is positioned so that its distal end 162 within vessel 66 is positioned at the opening aneurysm 64. Microcatheter 144 is provided with radiopaque marker 108 at distal tip 162, a tip marker. Moving toward the proximal end of microcatheter 144 is a second radiopaque marker 110, a proximal marker. Radiopaque markers 108 and 110 are, for example, in the form of radiopaque rings made of platinum, approximately 1-3 mm in longitudinal length along the axis of microcatheter 144. Rings 110 and 108 are typically separated by about 3 cm on microcatheter 144. Similarly, wire 10 has a radiopaque marker 112 defined on it such that marker 112 on wire 10 is approximately with aligned with marker 110 on microcatheter 14 when coil 56 is fully deployed into aneurysm 64. Typically, full deployment will place the solder or connection point 54 of the order of 2-3 mm past opening 68 of aneurysm 64. Distal marker 108 on microcatheter 144 is used to facilitate the location of the microcatheter tip, which can often be obscured by the coils which have been previously deployed. The coils are a varying lengths depending on the application or size of the aneurysm or vascular cavity being treated. Coil lengths of 4-40 cm are common. Therefore, even though the thinness of coil 56 may make it difficult to see under standard fluoroscopy and even though the fineness of wire 10 may similarly be obscured or partly obscured, radiopaque markers 108, 110 and 112 are clearly visible. Manipulation of wire 10 to proximal marker 110 can then easily be observed under conventional fluoroscopy even when there are some loss of resolution or fluoroscopic visual obstruction of the coil.

Further, in the previous embodiments, such as that shown in Figures 4 and 5, when electrothrombosis is used to form the occlusion within vascular aneurysm 64, coil 56 is used as the electrical anode while the cathode is a large skin electrode 72 typically conductively applied to the groin or scalp. Figure 9 illustrates an alternative embodiment wherein microcatheter 144 is supplied with an end electrode 114 coupled to an electrical conductor 116 disposed along the length of microcatheter 144. Wire 116 is ultimately led back to voltage source 70 so that ring electrode 114 is used as the cathode during electrothrombosis instead of an exterior skin electrode 72. With the embodiment of Figure 9, the electrical currents and electrical current paths which are set up during the electrothrombosis formation are local to the site of application which allows even smaller currents and voltages to be used to initiate electrothrombosis than in the situation when an exterior skin electrode must be utilized. The electrothrombosic current distributions are also better controlled and localized to the site of the thrombus formation. The possibility of stray thrombus formations occurring at unwanted sites or uncontrolled and possibly unwanted electrical current patterns being established elsewhere in the brain or body is therefore largely avoided.

Many alterations and modifications may be made by those having ordinary skill in the art without departing from the spirit and scope of the invention. Therefore, it must be understood that the shape of the tip or distal platinum coil used in combination with the wire according to the invention may be provided with a variety of shapes and envelopes. In addition thereto, the composition of the micro-guidewire tip may be made of elements other than platinum including

stainless steel, beryllium, copper and various alloys of the same with or without platinum. Still further, the diameter of the wire, various of the wire described above and the stainless steel coil immediately proximal to the detachable tip may be provided with differing diameters or cross sections to vary the times and current magnitudes necessary in order to effectuate electrolytic detachment from the tip. Still further, the invention may include conventional electronics connected to the proximal end of the wire for determining the exact instant of detachment of the distal tip from the wire.

Therefore, the illustrated embodiment has been set forth only for the purposes of clarity and example and should not be taken as limiting the invention as defined by the following claims, which include all equivalent means whether now known or later devised.

We claim:

1. A method for forming an occlusion within a vascular cavity having blood disposed therein comprising the steps of:

endovascularly disposing a wire near an endovascular opening into said vascular cavity;

disposing a distal tip of said wire into said vascular cavity to pack said cavity to mechanically form said occlusion within said vascular cavity about said distal tip; and

detaching said distal tip from said wire to leave said distal tip within said vascular cavity,

whereby said vascular cavity is occluded by said distal tip, and any thrombus formed by use of said tip.

2. The method of Claim 1 wherein said step of detaching said distal tip from said wire comprises the step of mechanically detaching said distal tip from said wire.

3. The method of Claim 1 where said wire and tip are used within a microcatheter and where in said step of detaching said distal tip from said wire, said

wire and tip are longitudinally displaced within said microcatheter, said microcatheter having a radio-opaque proximal marker, said wire and tip having collectively a single radio-opaque marker, said displacement of said wire and tip moving said single radio-opaque marker to the proximity of said proximal marker on said microcatheter when said tip is fully deployed.

4. The method of Claim 1 wherein said step of disposing said tip into said vascular cavity to pack said cavity comprises the step of disposing a tip having a plurality of filaments extending therefrom to pack said cavity.

5. The method of Claim 1 wherein said step of disposing said tip into said vascular cavity to pack said cavity comprises the step of disposing a long flexible tip folded upon itself a multiple number of times to pack said cavity.

6. A method for forming an occlusion within a vascular cavity having blood disposed therein comprising the steps of:

endovascularly disposing a wire within a microcatheter near an endovascular opening into said vascular cavity, said microcatheter having a distal tip electrode;

disposing a distal tip of said wire into said vascular cavity to pack said cavity to form said occlusion within said vascular cavity about said distal tip by applying a current between said electrode on said distal end of said wire packed into said cavity and said distal tip electrode on said microcatheter; and

detaching said distal tip from said wire to leave said distal tip within said vascular cavity,

whereby said vascular cavity is occluded by said distal tip, and any thrombus formed by use of said tip.

7. A wire for use in formation of an occlusion within a vascular cavity used in combination with a microcatheter comprising:

a core wire; and

a detachable elongate tip portion extending said core wire for a predetermined lineal extent adapted to being packed into said vascular cavity to form said occlusion in said vascular cavity and coupled to said distal portion of said core wire,

whereby endovascular occlusion of said vascular cavity can be performed.

8. The wire of Claim 7 wherein said elongate tip portion is a long and substantially pliable segment adapted to be multiply folded upon itself to substantially pack said vascular cavity.

9. The wire of Claim 7 wherein said elongate tip portion is a segment adapted to be disposed in said vascular cavity and having a plurality of filaments extending therefrom to substantially pack said vascular cavity when disposed therein.

10. The wire of Claim 7 wherein said microcatheter has a pair of radioopaque markers disposed thereon and wherein said core wire has a radioopaque marker disposed thereon, said marker on said core wire being positioned in the proximity of one of said pair of markers on said microcatheter when said core wire is deployed, said other marker on said microcatheter indicating the distal end of said microcatheter.

11. The wire of Claim 7 where said core wire and tip are coupled by polyester.

12. A microcatheter system for use in formation of an occlusion within a vascular cavity comprising:

a microcatheter having a distal end adapted for disposition in the proximity of said vascular cavity, said distal end having an electrode disposed thereon;

a conductive wire disposed in said microcatheter and longitudinally displaceable therein, said wire comprising:

a core wire; and

an elongate tip portion extending said core wire for a predetermined lineal extent adapted to being packed into said vascular cavity to form said occlusion in said vascular cavity and coupled to said distal portion of said core wire by means of applying a current between said tip portion and said electrode on said microcatheter when said tip portion is disposed into said vascular cavity,

whereby endovascular occlusion of said vascular cavity can be performed.

13. A method for forming an occlusion within a vascular cavity having blood disposed therein comprising the steps of:

disposing a body into said cavity to substantially impede movement of blood in said cavity; and

employing said body in said cavity to form said occlusion within said vascular cavity,

whereby said vascular cavity is occluded by said body.

14. The method of Claim 13 wherein said step of disposing said body in said vascular cavity comprises the step of packing said body to substantially obstruct said cavity.

15. The method of Claim 14 where said step of packing said cavity with said body comprises the step of obstructing said cavity with a detachable elongate wire tip multiply folded upon itself in said cavity.

16. The method of Claim 13 wherein said step of disposing said body into said vascular cavity comprises disposing in said vascular cavity means for slowing blood movement in said cavity to initiate formation of said occlusion in said cavity.

17. The method of Claim 14 where said step of packing said cavity with said body comprises the step of obstructing said cavity with a body having a compound filamentary shape.

18. The method of Claim 13 wherein said step of employing said body in said vascular cavity to form said occlusion comprises the step of applying an electrical current to said body.

19. The method of Claim 13 wherein said step of employing said body in said vascular cavity to form said occlusion comprises the step of mechanically forming said occlusion in said body.

20. The method of Claim 13 wherein said step of employing said body in said vascular cavity to form said occlusion comprises the step of applying an electrical current to said body and simultaneously mechanically forming said occlusion in said body.

21. The method of Claim 18 where said step of applying an electrical current to said body comprises the step of applying an electrical current between said body and an proximate electrode carried on a microcatheter used for disposing said body into said cavity.

22. A wire for use in formation of an occlusion within a vascular cavity used in combination with a microcatheter comprising:

a core wire;

a detachable elongate tip portion extending said core wire for a predetermined lineal extent adapted to being packed into said vascular cavity to form said occlusion in said vascular cavity and coupled to said distal portion of said core wire, said tip portion including a first segment for disposition into said cavity and a second segment for coupling said first portion to said core wire, said second segment being adapted to be electrolysized upon application of current; and

an insulating coating disposed on said first segment, said second segment being left exposed to permit selective electrolysis thereof,

whereby endovascular occlusion of said vascular cavity can be performed.

23. A method for forming an occlusion within a vascular cavity having blood disposed therein comprising the steps of:

endovascularly disposing a wire near an endovascular opening into said vascular cavity;

disposing a distal tip of said wire into said vascular cavity to pack said cavity to form said occlusion within said vascular cavity about said distal tip;

forming an electrothrombosis in said vascular cavity by applying current through said distal tip; and

mechanically detaching said distal tip from said wire to leave said distal tip within said vascular cavity,

whereby said vascular cavity is occluded by said distal tip, and any thrombus formed by use of said tip.

24. A method for forming an occlusion within a vascular cavity having blood disposed therein comprising the steps of:

endovascularly disposing a wire within a microcatheter near an endovascular opening into said vascular cavity;

disposing a distal tip of said wire into said vascular cavity to pack said cavity to form said occlusion within said vascular cavity about said distal tip by applying a current to said distal tip packed into said cavity; and

mechanically detaching said distal tip from said wire to leave said distal tip within said vascular cavity,

whereby said vascular cavity is occluded by said distal tip, and any thrombus formed by use of said tip.

IMPROVEMENTS IN AN ENDOVASCULAR ELECTROLYTICALLY DETACHABLE WIRE AND TIP FOR THE FORMATION OF THROMBUS IN ARTERIES, VEINS, ANEURYSMS, VASCULAR MALFORMATIONS AND ARTERIOVENOUS FISTULAS

Abstract of the Disclosure

An artery, vein, aneurysm, vascular malformation or arterial fistula is occluded through endovascular occlusion by the endovascular insertion of a platinum wire and/or tip into the vascular cavity. The vascular cavity is packed with the tip to obstruct blood flow or access of blood in the cavity such that the blood clots in the cavity and an occlusion if formed. The tip may be elongate and flexible so that it packs the cavity by being folded upon itself a multiple number of times, or may pack the cavity by virtue of a filamentary or fuzzy structure of the tip. The tip is then separated from the wire mechanically or by electrolytic separation of the tip from the wire. The wire and the microcatheter are thereafter removed leaving the tip embedded in the thrombus formed within the vascular cavity. Movement of wire in the microcatheter is more easily tracked by providing a radioopaque proximal marker on the microcatheter and a corresponding indicator marker on the wire. Electrothrombosis is facilitate by placing the ground electrode on the distal end of the microcatheter and flowing current between the microcatheter electrode and the tip.

FIG. 1

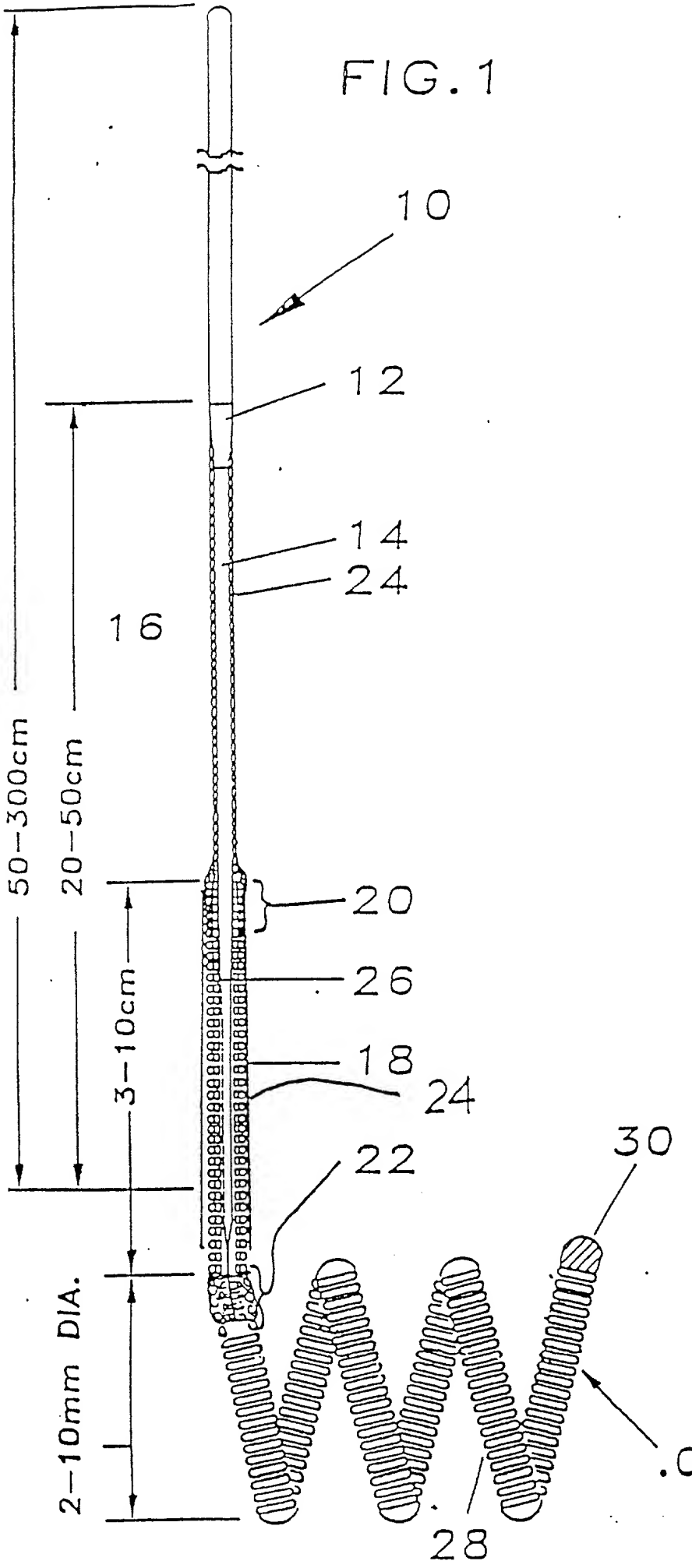
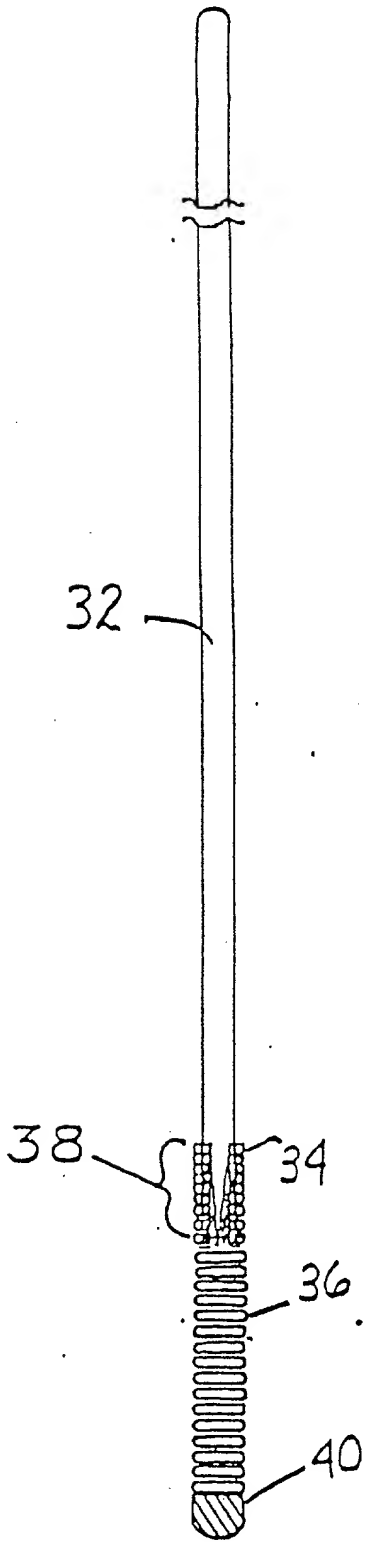


FIG. 2



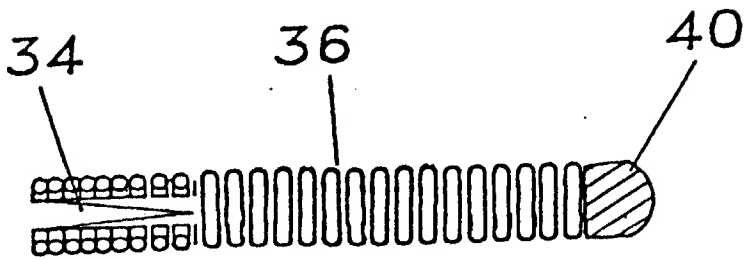


FIG. 2A

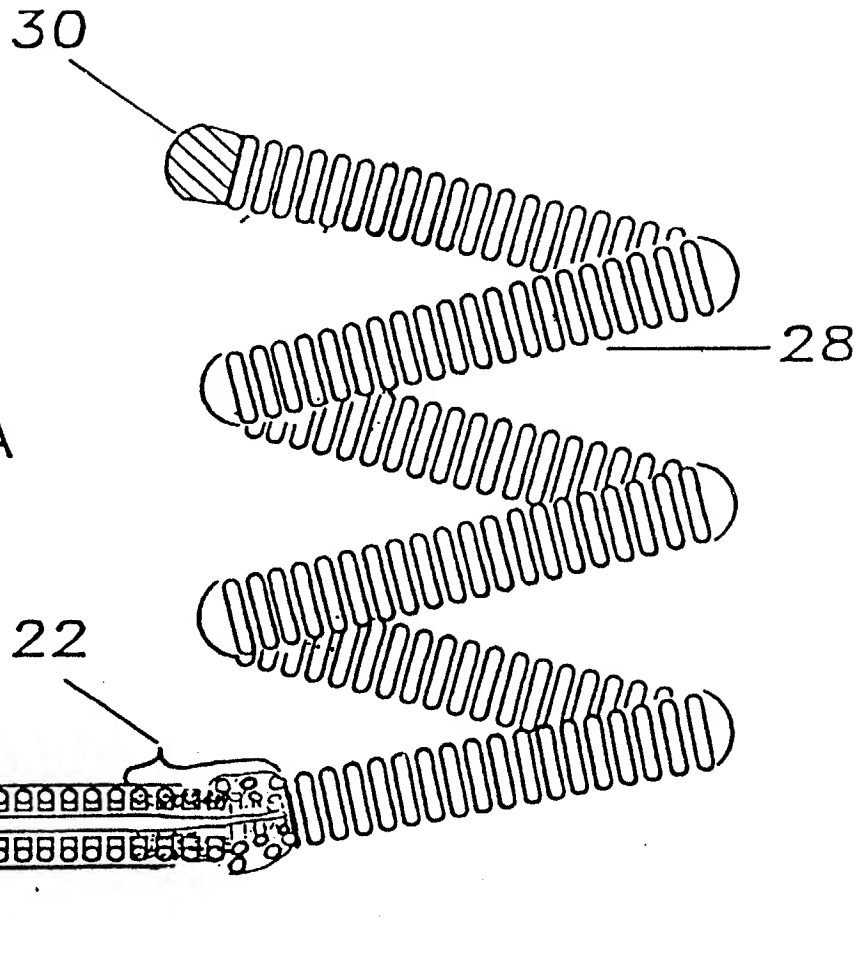


FIG. 1A

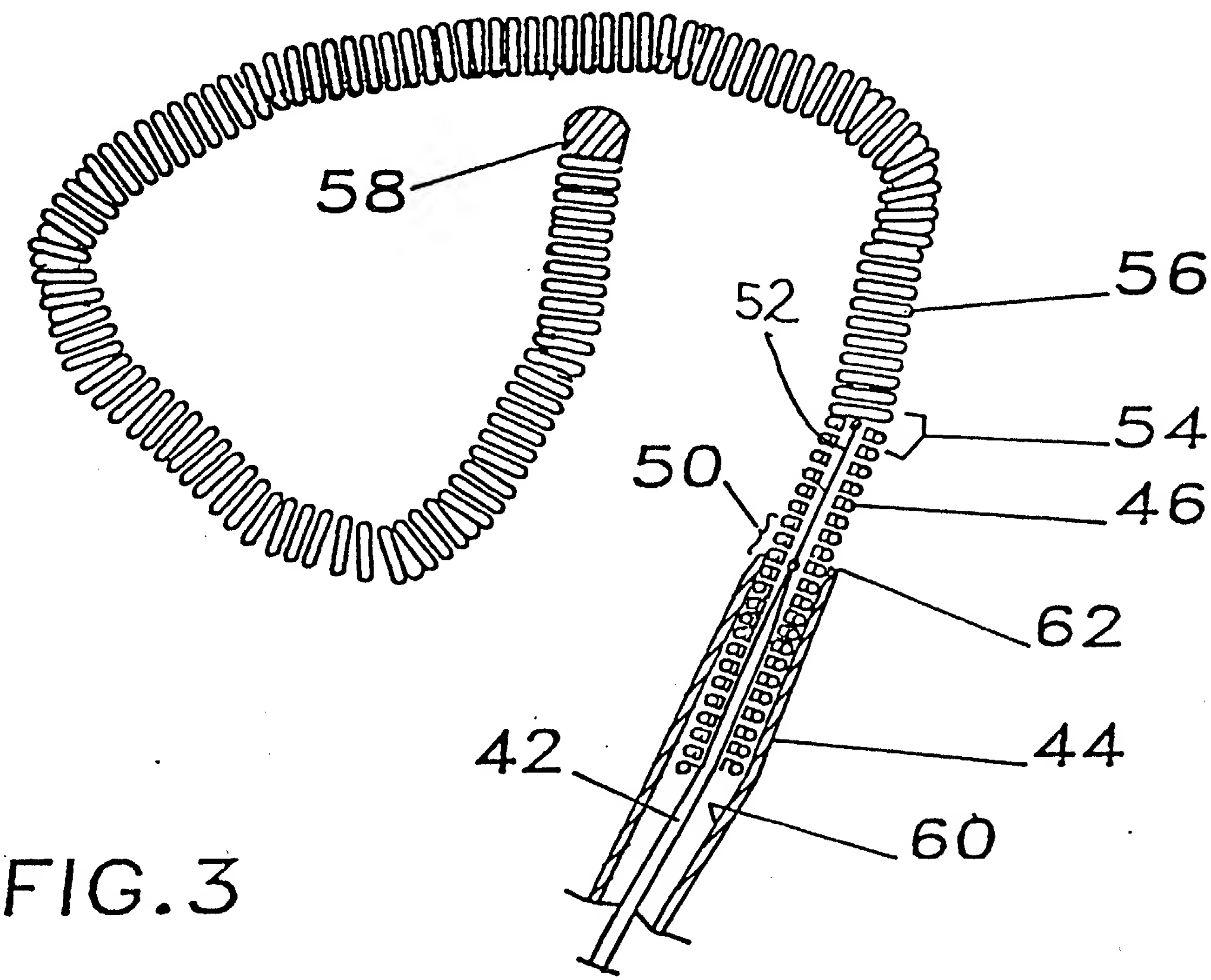


FIG.3

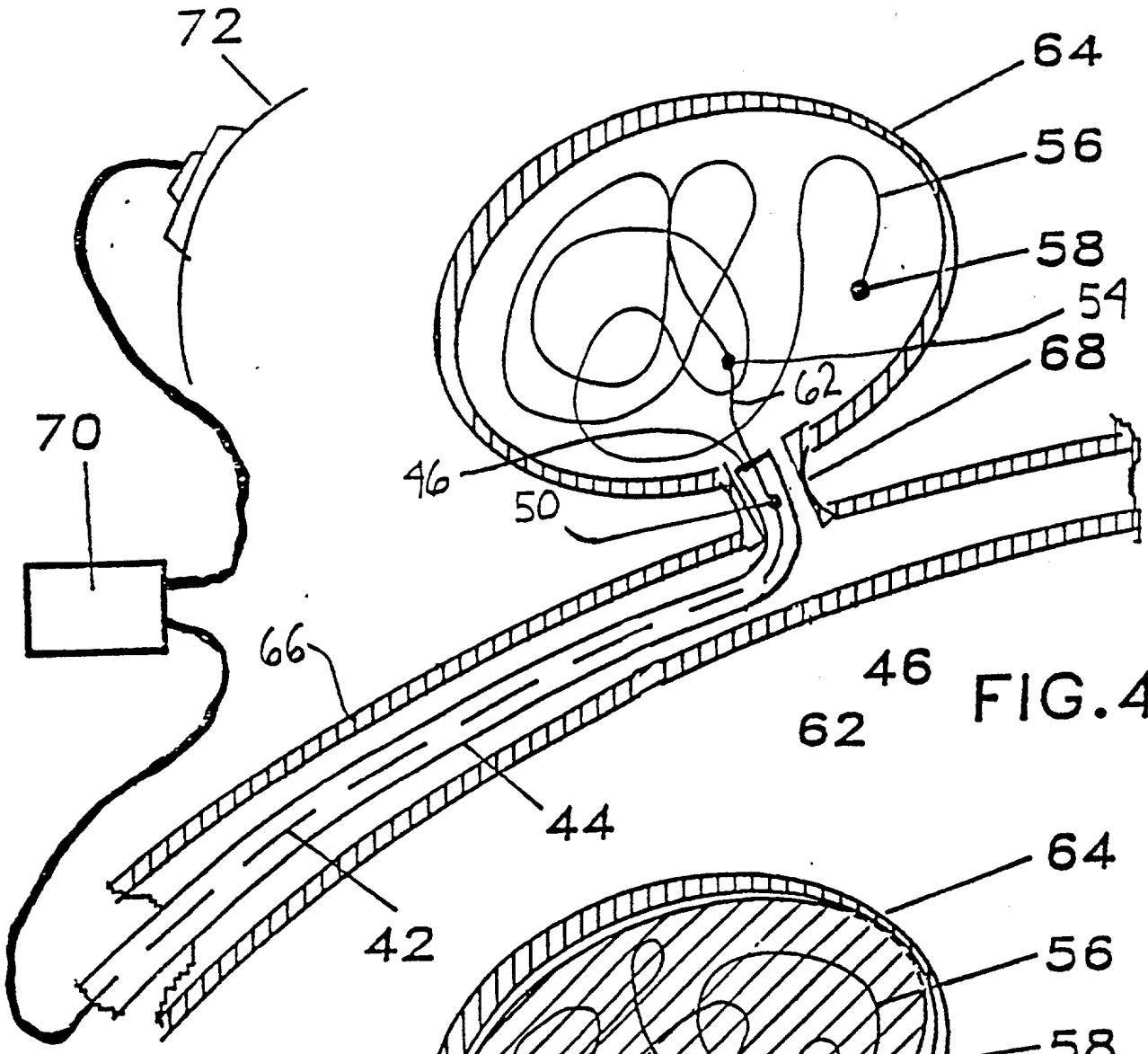

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FIG.4

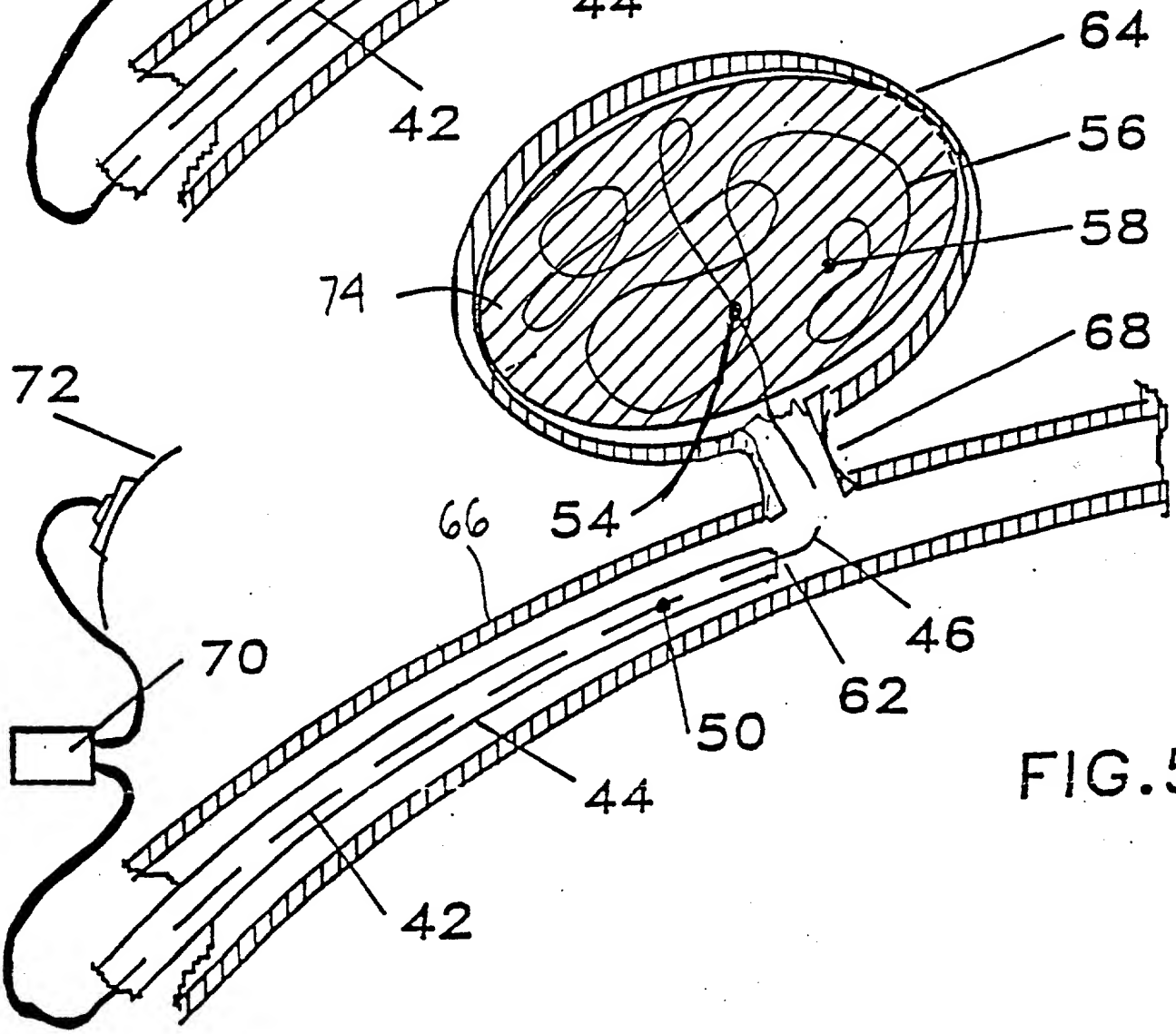
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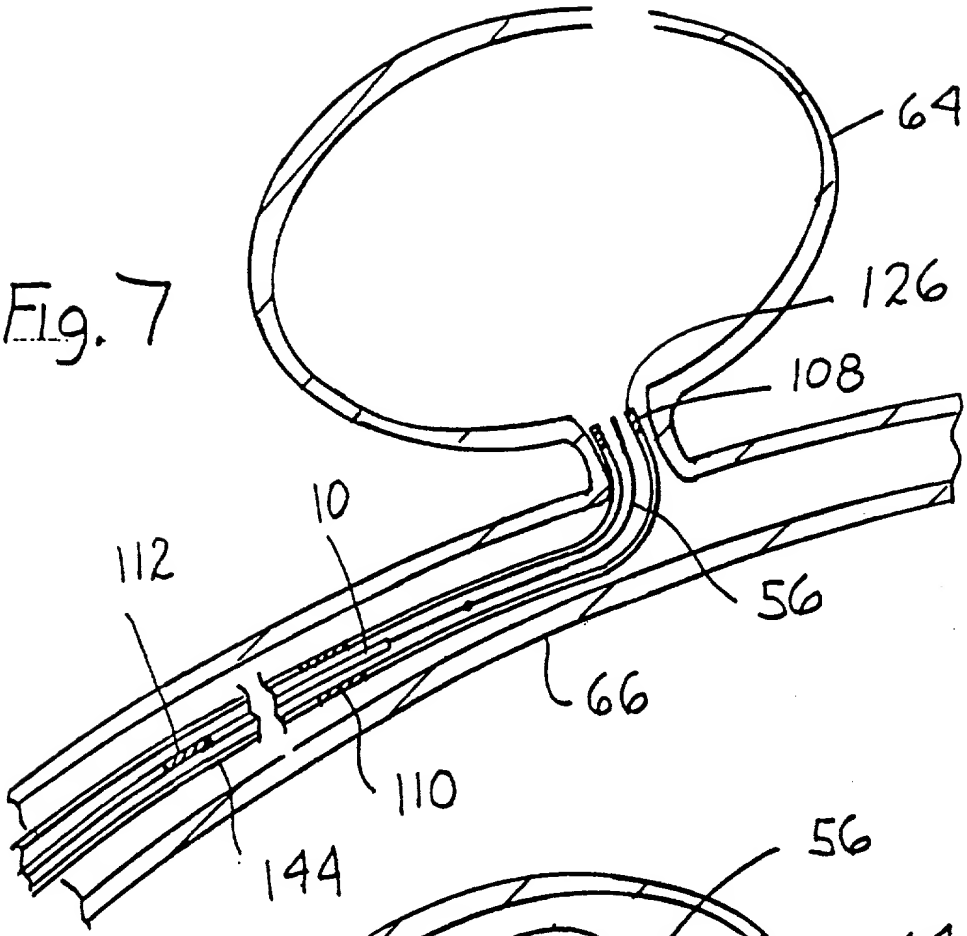
FIG.5

Fig. 7



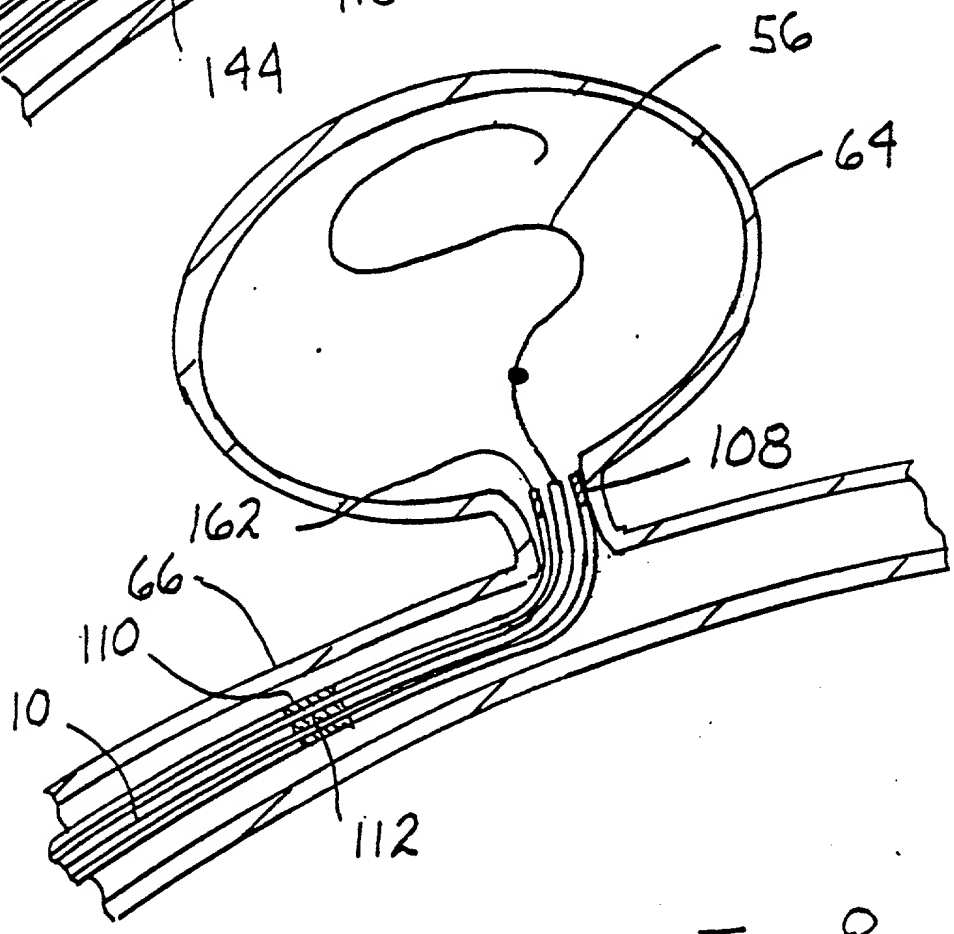
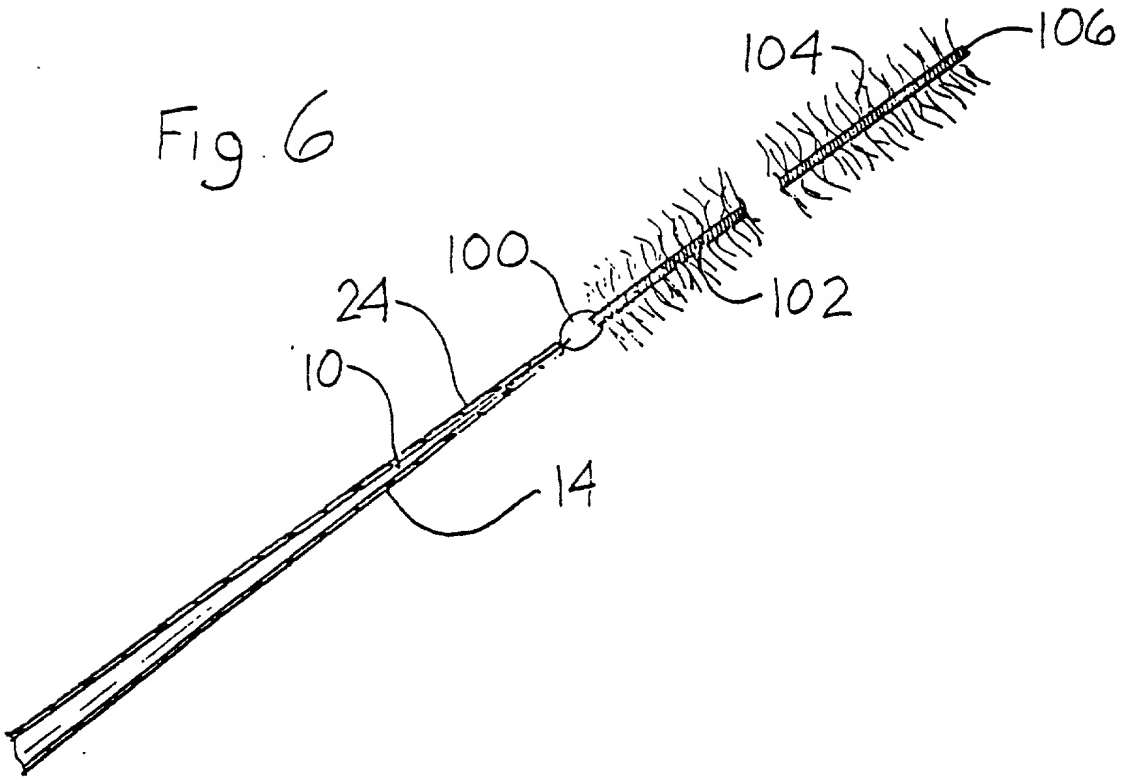


Fig 8

Fig. 6



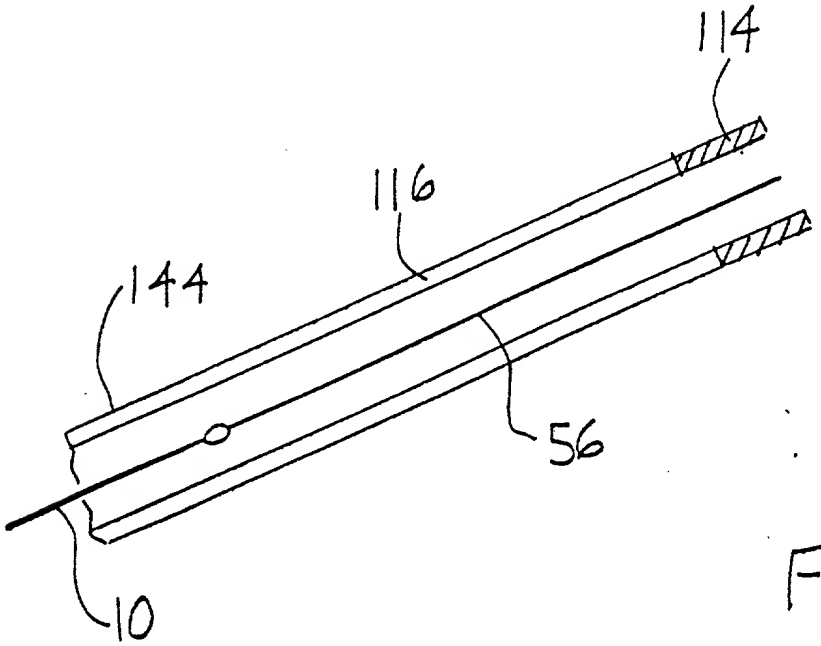


Fig. 9

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Guglielmi et al. (UC)
M203a-D
PATENT

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

APPLICANTS: GUIDO GUGLIELMI et al.

TITLE: IMPROVEMENTS IN AN ENDOVASCULAR ELECTROLYTICALLY DETACHABLE WIRE AND TIP FOR THE FORMATION OF THROMBUS IN ARTERIES, VEINS, ANEURYSMS, VASCULAR MALFORMATIONS AND ARTERIOVENOUS FISTULAS

I hereby certify that this correspondence is being deposited with the United States Postal Service as first class mail in an envelope addressed to: Commissioner of Patents and Trademarks, Washington, D.C. 20231, on FEB. 20, 1992
(Date of Deposit)
Maureen Vieira
MAUREEN VIEIRA
Date of Signature: Feb. 20, 1992

STATEMENT OF CANDOR

Hon. Commissioner of Patents and Trademarks
Washington, D.C. 20231

Dear Sir:

Pursuant to the rules of candor and ethics of the United States Patent Office, the undersigned states that the phrase "Vasoocclusion Coil with Attached Fiberous Elements, filed Oct. 2, 1991, serial number 07/771,013" at page 21, lines 9 and 10, and the word "may" at page 21, line 8, was added to the specification after the declaration was signed by the inventors.

A supplementary declaration will be filed at the appropriate time in the prosecution of the matter. The addition is not believed to be material to the disclosure of the specification or its patentability.

Respectfully submitted,

Daniel L. Dawes
Reg. 27123

100 Corporate Pointe, Ste 330
Culver City, California 90230
714 644 7740

DECLARATION AND POWER OF ATTORNEY

CONTINUATION-IN-PART APPLICATION

We, GUIDO GUGLIELMI, a citizen of Italy, and IVAN SEPETKA, a citizen of United States of America, declare that we verily believe that we are the original and first inventors of the IMPROVEMENTS IN AN ENDOVASCULAR ELECTROLYTICALLY DETACHABLE GUIDEWIRE TIP FOR THE FORMATION OF THROMBUS IN ARTERIES, VEINS, ANEURYSMS, VASCULAR MALFORMATIONS AND ARTERIOVENOUS FISTULAS, described and claimed in the continuation-in-part application attached hereto;

that this application in part discloses and claims subject matter disclosed in our earlier filed pending application, Serial No. 07/492,717 filed March 13, 1990;

that we hereby state that we have reviewed and understand the contents of the attached specification including the claims as amended;

that we acknowledge our duty to disclose information of which we are aware which is material to the examination of this application in accordance with Title 37, Code of Federal Regulations, Section 1.56(a);

that we acknowledge our duty to disclose material information as defined in Title 37, Code of Federal Regulations, Section 1.56(a) which occurred between the filing date of the prior application and the filing date of the continuation-in-part application which discloses and claims subject matter in addition to that disclosed in the prior application;

that as to the subject matter of this application which is common to said earlier application, we do not know and do not believe that the same was ever known or used in the United States of America before our invention thereof or patented or described in any printed publication in any country before our invention thereof or more than one year prior to said earlier application, or in public use or on sale in the United States of America more than one year prior to said earlier application; that said common subject matter has not been patented or made the subject of an inventor's certificate issued before the date of said earlier application in any country foreign to the United

States of America on an application filed by us or our legal representatives or assigns more than twelve months prior to said earlier application; and that no application for patent or inventors' certificate on said invention has been filed by us or our representatives or assigns in any country foreign to the United States of America except as follows:

none

that, as to the subject matter of this application which is not common to said earlier application, we do not know and do not believe that the same was ever known or used in the United States of America before our invention thereof or patented or described in any printed publication in any country before our invention thereof or more than one year prior to the date of this application, or in public use or on sale in the United States of America more than one year prior to the date of this application, and that said subject matter has not been patented or made the subject of an inventors' certificate issued in any country foreign to the United States of America on an application filed by us or our legal representatives or assigns more than twelve months prior to the date of this application; and that no application for patent or inventors' certificate on said invention has been filed by us or our representatives or assigns in any country foreign to the United States of America except as follows:

none

I hereby appoint the following attorney(s) and/or agent(s) to prosecute this application and to transact all business in the United States Patent and Trademark Office connected therewith:

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We hereby declare that all statements made herein of our own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the application or any patent issuing thereon.

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Date Signature of Inventor

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Date Signature of Inventor

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EM 601094898US

Applicant or Patentee: GUGLIELMI, G., et al.
Serial or Patent No.: _____ - Docket No. M203a-D
Filed or Issued: _____
For: IMPROVEMENTS IN AN ENDOVASCULAR ELECTROLYTICALLY DETACHABLE GUIDEWIRE TIP FOR THE FORMATIO OF THROMBUS IN ARTERIES, VEINS, ANEURYSMS, VASCULAR MALFORMATION AND ARTERIOVENOUS FISTULA

VERIFIED STATEMENT (DECLARATION) CLAIMING SMALL ENTITY STATUS
[37 CFR 1.9(f) and 1.27(d)] — NONPROFIT ORGANIZATION

I hereby declare that I am an official empowered to act on behalf of the nonprofit organization identified below:

NAME OF ORGANIZATION: The Regents of the University of California
ADDRESS OF ORGANIZATION: 300 Lakeside Drive, 22nd Floor
Oakland, CA 94612-3550

TYPE OF ORGANIZATION
[X] UNIVERSITY OR OTHER INSTITUTION OF HIGHER EDUCATION
[X] TAX EXEMPT UNDER INTERNAL REVENUE SERVICE CODE [26 USC 501(a) and 501(c) (3)]
[ ] NONPROFIT SCIENTIFIC OR EDUCATIONAL UNDER STATUTE OF STATE OR THE UNITED STATES OF AMERICA
(NAME OF STATE _____)
(CITATION OF STATUTE _____)
[ ] WOULD QUALIFY AS TAX EXEMPT UNDER INTERNAL REVENUE SERVICE CODE [26 USC 501(a) and 501(c) (3)] IF LOCATED IN THE UNITED STATES OF AMERICA
[ ] WOULD QUALIFY AS NONPROFIT SCIENTIFIC OR EDUCATIONAL UNDER STATUTE OF STATE OF THE UNITED STATES OF AMERICA IF LOCATED IN THE UNITED STATES OF AMERICA
(NAME OF STATE _____)
(CITATION OF STATUTE _____)

I hereby declare that the nonprofit organization identified above qualifies as a nonprofit organization as defined in 37 CFR 1.9(e) for purposes of paying reduced fees under section 41(a) or (b) of Title 35, United States Code with regard to the invention entitled IMPROVEMENTS IN AN ENDOVASCULAR ELECTROLYTICALLY DETACHABLE GUIDEWIRE TIP FOR THE FORMATION FO THROMBUS IN ARTERIES, VEINS, ANEURYSMS, VASCULAR MALFORMATION AND ARTERIO- by inventor(s) VENOUS FISTULAS
by inventors Guido Guglielmi and Ivan Sepetka described in

[X] the specification filed herewith
[ ] application serial no. _____, filed _____
[ ] Patent no. _____, issued _____

I hereby declare that rights under contract or law have been conveyed to and remain with the nonprofit organization with regard to the above identified invention.

If the rights held by the nonprofit organization are not exclusive, each individual, concern, or organization having rights to the invention is listed below* and no rights to the invention are held by any person, other than the inventor, who would not qualify as an independent inventor under 37 CFR 1.9(c) if that person made the invention, or by any concern which would not qualify as a small business concern under 37 CFR 1.9(d) or a nonprofit organization under 37 CFR 1.9(e).
*NOTE: Separate verified statements are required from each named person, concern or organization having rights to the invention averring to their status as small entities (37 CFR 1.27).

NAME TARGET THERAPEUTICS
ADDRESS 130 Via Robles, San Jose, California 95134
[ ] INDIVIDUAL [X] SMALL BUSINESS CONCERN [ ] NONPROFIT ORGANIZATION

NAME _____
ADDRESS _____
[ ] INDIVIDUAL [ ] SMALL BUSINESS CONCERN [ ] NONPROFIT ORGANIZATION

I acknowledge the duty to file, in this application or patent, notification of any change in status resulting in loss of entitlement to small entity status prior to paying, or at the time of paying, the earliest of the issue fee or any maintenance fee due after the date on which status as a small entity is no longer appropriate. [37 CFR 1.28(b)]

I hereby declare that all statements made of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like are punishable by fine or imprisonment, or both, under 18 USC § 1001, and may jeopardize the validity of the application, any patent issuing thereon, or any patent to which this verified statement is directed.

NAME OF PERSON SIGNING Valentin Fikovsky
TITLE IN ORGANIZATION Manager, Engineering Licensing, Office of Technology Transfer
ADDRESS OF PERSON SIGNING 300 Lakeside Drive, 22nd Floor
Oakland, California 94612-3550

SIGNATURE Valentin Fikovsky DATE January 29, 1992

TAT 16

UC Case No.: 89-203-2

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EM601094898US

Applicant or Patentee: GUGLIELMI, G., et al.
Serial or Patent No.:
Filed or Issued:
For: IMPROVEMENTS IN AN ENDOVASCULAR ELECTROLYTICALLY DETACHABLE WIRE AND TIP FOR THE FORMATION OF THROMBUS IN ARTERIES, VEINS, ANEURYSMS, VASCULAR MALFORMATIONS AND ARTERIOVENOUS FISTULAS
Attorney's Docket No.: M203a-D

VERIFIED STATEMENT (DECLARATION) CLAIMING SMALL ENTITY STATUS
(37 CFR 1.9(f) and 1.27(c)) - SMALL BUSINESS CONCERN

I hereby declare that I am

[ ] the owner of the small business concern identified below:
[X] an official of the small business concern empowered to act on behalf of the concern identified below:

NAME OF CONCERN TARGET THERAPEUTICS
ADDRESS OF CONCERN 130 Via Robles
San Jose, California 95134

I hereby declare that the above identified small business concern qualifies as a small business concern as defined in 13 CFR 121.3-18, and reproduced in 37 CFR 1.9(d), for purposes of paying reduced fees under section 41(a) and (b) of Title 35, United States Code, in that the number of employees of the concern, including those of its affiliates, does not exceed 500 persons. For purposes of this statement, (1) the number of employees of the business concern is the average over the previous fiscal year of the concern of the persons employed on a full-time, part-time or temporary basis during each of the pay periods of the fiscal year, (2) concerns are affiliates of each other when either, directly or indirectly, one concern controls or has the power to control the other, or a third party or parties controls or has power to control both.

I hereby declare that rights under contract or law have been conveyed to and remain with the small business concern identified above with regard to the invention, entitled IMPROVEMENTS IN AN ENDOVASCULAR ELECTROLYTICALLY DETACHABLE WIRE ANE TIP ... by inventor(s) Guido Guglielmi and Ivan Sepetka described in

[X] the specification filed herewith
[ ] application serial no. _____, filed _____.
[ ] patent no. _____, issued _____.

If the rights held by the above identified small business concern are not exclusive, each individual, concern or organization having rights to the invention is listed below* and no rights to the invention are held by any person, other than the inventor, who could not qualify as a small business concern under 37 CFR 1.9(d) or by any concern which would not qualify as a small business concern under 37 CFR 1.9(d) or a nonprofit organization under 37 CFR 1.9(e). *NOTE: Separate verified statements are required from each named person, concern or organization having rights to the invention averring to their status as small entities. (37 CFR 1.27)

NAME THE REGENTS OF THE UNIVERSITY OF CALIFORNIA
ADDRESS 300 Lakeside Drive, 22nd Floor, Oakland, CA 94612-3550
[ ] INDIVIDUAL [ ] SMALL BUSINESS CONCERN [X] NONPROFIT ORGANIZATION

NAME
ADDRESS
[ ] INDIVIDUAL [ ] SMALL BUSINESS CONCERN [ ] NONPROFIT ORGANIZATION

I acknowledge the duty to file, in this application or patent, notification of any change in status resulting in loss of entitlement to small entity status prior to paying, or at the time of paying, the earliest of the issue fee or any maintenance fee due after the date on which status as a small entity is no longer appropriate. (37 CFR 1.28(b))

I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under section 1001 of Title 18 of the United States Code, and that such willful false statements may jeopardize the validity of the application, any patent issuing thereon, or any patent to which this verified statement is directed.

NAME OF PERSON SIGNING Eric Engelson
TITLE OF PERSON OTHER THAN OWNER Vice-President, Target Therapeutics
ADDRESS OF PERSON SIGNING 130 Via Robles
San Jose, CA 95134
SIGNATURE _____ DATE 2/7/92